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REMARKS

At the time of the present Office Action, the present application had Claims 41-55 under consideration. Claims 1-40 were previously cancelled. Indeed, the above-identified application has had a long history of prosecution and claim amendments. The presently rejected Claims were principally introduced into prosecution upon the filing of a second submission under 37 C.F.R. §1.129(a) dated December 23, 1998. Applicants have outlined the history of the claim amendments below.

The application was filed on August 10, 1990, with 21 original Claims. A preliminary amendment dated September 23, 1991, cancelled Claim 1 and added new Claim 22. Amendments were made to Claims 2, 3, 4, 5, 6, 7, 8, 9, 10 and 11.

In the response submitted April 24, 1992, Claims 2, 3 and 18 were canceled and Claims 4, 5, 6, 7, 9, 10, 12, 14, 15, 17 and 19 were amended. Further, Claims 20 - 22 were cancelled and essentially rewritten as new Claims 23 - 26.

A further amendment was submitted December 15, 1992, wherein Claims 6, 7, 10, 11, 12, 14, 17, 23 and 26 were amended. In response to a Final Office Action dated March 2, 1993, Claims 9, 14, 17, 19, 23, 24, 25, and 26 were amended and concurrently a Notice of Appeal was filed. An advisory action dated September 27, 1993 indicated the amendment filed in response to the final rejection would not be entered and the Claims remained rejected. An appeal brief was filed March 2, 1994. In response to the Appeal, Appellants received a further non-final Office Action. In reply, Claim 17 was cancelled; Claims 12, 14, 15, 19, 23, 24, 25 and 26 were amended; and Claims 27 - 29 were added.

On July 7, 1995, in response to a Final Office Action dated Feb 14, 1995, Appellants cancelled Claim 16 and amended Claims 9, 12, 19, 23, 24, 25, 26 and 27. The amendment was entered, but the claims remained rejected. A Notice of Appeal was filed. Subsequently, on October 16, 1995, a response was filed under 37 C.F.R. §1.129(a). A Preliminary Amendment filed November 28, 1995 added new Claims 30 - 33. A further amendment dated April 17, 1996 was filed, wherein Claims 4, 13, 14, 19, 23, 24, 25, 26, 28, 29, 30 and 33 were amended and Claims 34 - 37 were added. A non-final Office Action dated September 4, 1996 again

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rejected pending Claims 4 - 7, 9 - 15, 19, and 23 - 37. In response, Claims 11, 15, 26 - 28 and 36 - 37 were Canceled; claims 4, 5, 6, 7, 9, 10, 12, 13, 14, 23, 29, 30, 34 and 35 were amended and Claims 38 - 40 were added. A Final Office Action dated April 1, 1997 was received, and Appellants filed a Notice of Appeal on Oct. 1, 1997, indicating that the rejections of Claims 7, 9 - 10, 12 - 14, 19, 23 - 25, 29 - 35 and 38 - 40 were to be appealed. However, Appellants did not file an Appeal Brief. When a new representative for Appellants reviewed the file, it was discovered that the application was actually abandoned due to filing the October 16, 1995, 37 C.F.R. §1.129(a) submission subsequent to filing the March 1994 Appeal Brief. On December 23, 1998, Appellants filed a timely petition to revive the unintentionally abandoned application and to accept the first submission made under 37 C.F.R. §1.129(a). Additionally, Appellants filed a second submission under 37 C.F.R. §1.129(a) which included an amendment canceling the pending Claims, 4 - 7, 9 - 10, 12 - 14, 19, 23 - 25, 29 - 35 and 38 - 40 and submitting new Claims 41 - 53. Appellants were notified in a communication from the Petitioner's Office dated August 9, 1999 that (i) the petition to revive the abandoned application was granted; (ii) the rules were waived with respect to the first submission under 37 C.F.R. §1.129(a) and said submission was accepted; and (iii) the second submission under 37 C.F.R. §1.129(a) was accepted.

In response to an Office Action dated June 27, 2000, Claims 44, 49 and 51 were amended. A further amendment was filed July 24, 2001, wherein Claims 41, 45, 47, 48 and 50 were amended and Claims 54 and 55 were added. In Response to a Final Office Action dated October 23, 2001, Applicants filed a Notice of Appeal and subsequent Appeal Brief regarding the rejection of Claims 41 - 55. Pursuant to a decision by the Board of Patent Appeals and Interferences mailed December 24, 2003, prosecution of the present case was reopened, due to the vacating of the Examiner's rejections and remand to the Examiner by the Board. In the present Response, in order to further Applicants' business interests and the prosecution of the present application, yet without acquiescing to the Examiner's arguments, Applicants have cancelled Claims 41-47, 49, 51, and 52, and amended Claims 48, 50, and 54. Applicants expressly reserve the right to pursue these and/or broader and/or narrower Claims in subsequently filed applications. The Examiner's current rejections are addressed in the following order:

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- 1) Claims 41-55 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the written description requirement;
- 2) Claim 48 stands rejected under 35 U.S.C. §102(b), as allegedly being anticipated; and
- 3) Claims 41, 42, 45-47, 50, and 52 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious.

1) The Written Description Requirement is Met

The Examiner has rejected Claims 41-55 under 35 U.S.C. §112, first paragraph as allegedly not meeting the written description requirement. As Claims 41-47, 49, and 51-52 have been cancelled, the Examiner's rejection with regard to these Claims is moot. Thus, Applicants herein only address the rejection as it pertains to Claims 48, 50, and 53-55.

The Examiner argues that "[t]he scope of Claim 48 is highly variant and includes many chromosomal intracellular or extracellular wild-type protease genes that are to be deleted in the claimed *Bacillus* host, where the genes have widely differing intracellular or extracellular wild-type serine proteases, metalloproteases, cysteine proteases, threonine proteases and aspartyl proteases." (Office Action, page 6). Similar arguments are presented by the Examiner with regard to the remaining Claims.

While Applicants must respectfully disagree with the Examiner's arguments, as indicated above, Applicants have amended Claim 48 without prejudice to recite that the alkalophilic strain is a *Bacillus* novo species PB92 or the derivative PBT 110, and that the high alkaline protease is a high alkaline serine protease. Support for these amendments is provided throughout the Specification as filed. Thus, no new matter is presented in these amendments. Applicants respectfully submit that the Specification as filed provides more than sufficient disclosure to show that the inventors were in possession of the claimed invention at the time of filing. Thus, Applicants respectfully request that this rejection be withdrawn.

2) The Claims are Novel

The Examiner has rejected Claim 48 under 35 U.S.C. §102(b), as allegedly being anticipated by Fahnestock *et al.* (Fahnestock *et al.*, Appl. Environ. Microbiol., 53:379-384 [1987]).

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Applicants must respectfully disagree. Nonetheless, as indicated above, Claim 48 has been amended without prejudice. As the cited reference does not contain each and every element of the amended Claim 48², Applicants respectfully submit that this reference does not anticipate Claim 48. Thus, Applicants respectfully request that this rejection be withdrawn.

3) The Claims are Unobvious

The Examiner has rejected Claims 41, 42, 45-47, 50, and 52 under 35 U.S.C. §103(a) as allegedly being unpatentable over Fahnestock *et al.*, in view of Takagi *et al.* (Takagi *et al.*, J. Biol. Chem., 263:19592-19596 [1988]).

In particular, the Examiner argues that with regard to Claims 41, 42 and 45-47, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by Fahnestock *et al.* where the *Staphylococcus aureus* *apa-1* gene, present in a plasmid contained in the protease-deficient *Bacillus* strains due to chromosomal deletion of the subtilisin structural gene (*apr*), is replaced with the gene encoding a mutant subtilisin E with enhanced protease activity taught by Takagi *et al.*, and the protease-deficient *Bacillus* strains taught by Fahnestock *et al.* are used to express and accumulate the mutant subtilisin E." (Office Action, page 11). The Examiner further argues that one of skill in the art "would have been motivated to do this because Fahnestock *et al.* teach that [sic] advantage that these protease-deficient *Bacillus* host strains are superior host strains for the production of foreign proteins since the reduced protease levels allows for the accumulation of produced foreign proteins with less degradation." (Office Action, page 12). With regard to expectation of success, the Examiner argues that there would be a reasonable expectation of success because "Fahnestock *et al.* teach the successful higher production and accumulation of

² Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . . There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Fdn. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

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staphylococcal protein A in the taught protease-deficient *Bacillus* host strains.”
(Office Action, page 12).

With regard to Claims 50 and 52, the Examiner argues that the invention “was within the ordinary skill in the art to make and use at the time [the invention] was made” (Office Action, page 11).

Applicants must respectfully disagree with the Examiner’s rejections and rationale. In regards to obviousness, Applicants contend that an obviousness rejection must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, all of the facts must be considered, and the Examiner must supply the factual basis for the rejection. The Examiner may not, because she doubts that the invention is patentable, resort to speculation, unfounded assumptions, or hindsight reconstruction to supply deficiencies in the factual basis for the rejection. See, *In re Warner*, 379 F.2d 1011, 154 USPQ 173 (CCPA 1967). Furthermore, as stated by the Federal Circuit, (*W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550, 220 USPQ 303, 311 [Fed. Cir. 1983]):

To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Applicants believe that this may be the situation in the present case. Whether taken alone or in combination, the prior art references cited by the Examiner do not provide any teaching or suggestion of the claimed invention. A *prima facie* case of obviousness requires the Examiner to cite to a combination of references which (a) suggests or motivates one of skill in the art to modify their teachings to yield the claimed invention, (b) discloses the elements of the claimed invention, and (c) provides a reasonable expectation of success should the claimed invention be carried out. Failure to establish any one of these requirements precludes a finding of a *prima facie* case of obviousness and, without more, entitles Applicant to withdrawal of the rejection of the claims in issue.³ Applicants respectfully submit that neither of the references taken alone or in combination provides any suggestion or motivation to

³ See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990); *In re Dow Chemical Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988).

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combine their teachings, nor does this combination result in the presently claimed invention, as all of the elements are not disclosed by the prior art. Indeed it is axiomatic for establishing a *prima facie* case of obviousness that "all the claim limitations must be taught or suggested by the prior art."⁴ In addition, there is no reasonable expectation of success that the combination of the Patents would result in the presently claimed invention.

Furthermore, an essential requirement for a *prima facie* case of obviousness is whether a person skilled in the art would be motivated to modify the reference to arrive at the claimed invention.⁵ In particular,

"the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed."⁶

As indicated above, there is no teaching in these references, taken alone or in combination that would lead one of ordinary skill in the art to practice each and every element of the claimed invention. The Examiner may not utilize hindsight to argue that the claimed invention is obvious under the prior art references. As there is no teaching in either of these references that suggests or motivates their combination, nor even all of the elements of the claimed invention, Applicants respectfully submit that the Claims are unobvious and request that this rejection be withdrawn.

⁴ MPEP § 2143.03, citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

⁵ *In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988) and *In re Jones*, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992).

⁶ (Emphasis added) *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998); *Robotic Vision Systems Inc. v. View Engineering Inc.*, 51 USPQ2d 1948 (Fed. Cir. 1999).


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CONCLUSION

All grounds of rejection and objection of the Office Action of April 26, 2004, having been addressed, reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned at (650) 846-5838.

Respectfully submitted,

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